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INTERNATIONAL PRELIMINARY EXAMINATION REPORT  
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference Case 21568	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP 03/14723	International filing date (day/month/year) 22.12.2003	Priority date (day/month/year) 13.01.2003
International Patent Classification (IPC) or both national classification and IPC C07D311/72		
Applicant DSM IP ASSETS B.V et al.		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 5 sheets, including this cover sheet.  
  
☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).  
  
 These annexes consist of a total of    sheets.

- This report contains Indications relating to the following items:
  - I ☒ Basis of the opinion
  - II ☐ Priority
  - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV ☐ Lack of unity of invention
  - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI ☐ Certain documents cited
  - VII ☐ Certain defects in the international application
  - VIII ☐ Certain observations on the international application

Date of submission of the demand  27.07.2004	Date of completion of this report  21.03.2005
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Lüdemann, S  Telephone No. +49 89 2399-7842 

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/EP 03/14723**

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-14 as originally filed

**Claims, Numbers**

1-16 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims	1-16
	No: Claims	-
Inventive step (IS)	Yes: Claims	1-16
	No: Claims	-
Industrial applicability (IA)	Yes: Claims	1-16
	No: Claims	-

**2. Citations and explanations**

**see separate sheet**

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EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP 03/14723

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

1. Reference is made to the following documents:

- D1: SCHNEIDER M ET AL: 'Industrial application of Nafion-systems in rearrangement-aromatisation, transesterification, alkylation, and ring-closure reactions' APPLIED CATALYSIS A: GENERAL, ELSEVIER SCIENCE, AMSTERDAM, NL, vol. 220, no. 1-2, 25 October 2001 (2001-10-25), pages 51-58, XP004308362 ISSN: 0926-860X
- D2: WO 96/19288 A (DU PONT) 27 June 1996 (1996-06-27)
- D3: INOUE S ET AL: 'Improved general method of ortho alkylation of phenols using alkyl isopropyl sulfide, sulfonyl chloride, and triethylamine. An expedient synthesis of representative oxygen heterocycles and (2R,4'R,8'R)-[alpha]-tocopherol' JOURNAL OF ORGANIC CHEMISTRY 1987 UNITED STATES, vol. 52, no. 24, 1987, pages 5495-5497, XP001181392 ISSN: 0022-3263
- D4: WO 98/21197 A (HOFFMANN LA ROCHE) 22 May 1998 (1998-05-22)
- D5: US-A-6 048 988 (HAHN RAINER ET AL) 11 April 2000 (2000-04-11)

2. Novelty and inventive step (Art. 33(2) and (3) PCT)

- 2.1 D1 discloses a method for producing alpha-tocopherol, not alpha-tocopherol-acetate, from trimethylhydroquinone-diacetate, -1-monoacetate or trimethylhydroquinone with addition of isophytol by catalysis with Nafion (see scheme 1 and p.52, left col., second paragraph). Nafion is a perfluorinated sulphonic acid ion-exchange polymer.
- 2.2 D2 (reference 5 in D1) discloses an alternative Nafion catalysts entrapped within a porous metal oxide. D2 on p. 6, lines 29-33, discloses that these metal oxides could comprise metallic or semimetallic oxide compounds, such as e.g. Yttrium or copper oxides. However, D2 does not disclose metal salts of the formula  $M^{n+}(R^1SO_3^-)_n$  as used in the process of the present invention. D2 also does not disclose the process of claim 1.

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- 2.3 D3 discloses the production of alpha-tocopherol-esters in which the mono- or diester of a hydroquinone is reacted with an allyl alcohol derivative or an allyl alcohol, i.e. phytols, in the presence of zinc halides and proton-liberating acids.
- 2.4 D4 and D5 are less pertinent documents.
- 2.5 The subject-matter of claim 1 refers to a process for producing alpha-tocopherol-acetate from trimethylhydroquinone-monoacetate with addition of compounds selected from the group consisting of phytol, isophytol or (iso-)phytol derivatives by catalysis with a catalyst of the formula  $M^{n+}(R^1SO_3^-)_n$ .
- 2.6 The difference between the process of claim 1 and D3, which is considered as the closest prior art, is that a different catalyst is used.
- 2.7 Thus, the subject-matter of claim 1 is novel over D1-D3. Therefore, claim 1 is considered to meet the requirements of Art. 33(2) PCT.
- 2.8 The problem to be solved by the present application in view of D3 is the provision of an alternative process of manufacture of alpha-tocopherol-acetate from trimethylhydroquinone-acetate and isophytol. The problem is solved by catalysis with an alternative catalyst of the formula  $M^{n+}(R^1SO_3^-)_n$ .
- 2.9 Documents D1-D5 do not provide any teaching, motivation or suggestion, neither alone nor in combination, for the catalyst of claim 1. Therefore, the subject-matter of claim 1 is also considered to meet the requirements of Art. 33 (3) PCT.
- 2.10 The dependent claims 2-16 add features to the process of claim 1 and thus also relate to novel and inventive subject-matter.
- 2.11 Claims 1-16 fulfill the requirements of industrial applicability (Art. 33(4)).